Exhibit 2

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing (*day/month/year*) 14 APR 2005

FOR FURTHER ACTION
See paragraph 2 below

Applicant's or agent's file reference		
639-C-PCT		
International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/23099	16 July 2004 (16.07.2004)	16 July 2003 (16.07.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): C08B and US Cl.: 536/056

Applicant

SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450	James O Wilson
Facsimile No. (703) 305-3230	Telephone No. 703-308-1235

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/23099

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/23099

Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 5,8-13	YES
	Claims 1-4, 6, 7	NO
Inventive step (IS)	Claims 1-4, 6, 7	YES
	Claims 5, 8-13	NO
Industrial applicability (IA)	Claims 1-13	YES
	Claims NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

Form PCT/ISA/237 (Box No. V) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/23099

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 5, 8-13 meet the criteria set out in PCT Article 33(2), because the prior art does not explicitly teach these compounds.

Claims 1-4, 6,7 meet the criteria set out in PCT Article 33(3), thus having an inventive step.
Claims 1-13 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.
Claims 1-4, 6, 7 do not meet the criteria set out in PCT Article 33(2), because James et al. (US 5,849,720) teach these compounds.. James et al. teach a composition comprising an effective amount of orally administered glucan, that is 1,3-1, 6 or 1,3-1, 4 mixed linkages that is capable of enhancing efficacy of antibodies (see column 4, lines 54-64). James et al. teach the use of said composition paired with a pharmaceutically acceptable carrier (see column 5, example 1). James et al. teach glucan derived from yeast, bacteria, fungi, and plants (column 1, lines 13-15). James et al. teach the glucan to be of a high molecular weight ranging from 10,000 to 500,000 daltons (column 4, lines 23-25), which is stable to heat treatment (see Examples 1 and 2, column 5 and 6).

Claims 5, 8-13 do not meet the critera set out in PCT Article 33(3), thus lacking an inventive step in view Jamas et al (US 5,849,720), Dorothee Herlyn (US 5,130,127), Yan et al. (" Beta-glucan, a "specific" biologic response modifier that uses antibodies to target tumors for cytotoxic recognition by leukocyte complement receptor Type 3," Journal of immunology, 1999, Vol. 163, pp. 3045-3052), Dante J. Marciani (US 6,573,245), Cheever et al. (US 6,664,370), Chu et al. (Pub No. 2004/0109857), and Lane et al. (Pub No. 2003/0180254).
As discussed above, James et al teach the limitations of claims 1-4. Jamas et al. does not teach the limitations found in claims 5 and 8-13 as stated above. Dorothee Herlyn teaches a monoclonal tumor-binding antibody against cancer (column 1, lines 11-55), which is capable of activating complement (column 3, lines 40-45). Dorothee Herlyn teaches an antibody capable of activating the antibody dependent cell-mediated cytotoxicity (column 2, lines 25-30). Additionally, Dorothee Herlyn teaches the cancer to be melanoma or colon cancer (column 3, lines 55-57, claims 10 and 11).
As relating to claim 74 and 75, Yan et al. teach the antibody directed to a peptide, protein, RNA ,DNA or plasmid (page 12, middle paragraph, and page 14, last paragraph), and specifically, to ganglioside GD2 (page 12, middle paragraph).
As relating to claim 76, Chu et al. teach the antigen to be CD20 (page 15, paragraph 96 and table 4).
As relating to claim 77, Cheever et al. teach the antigen to be HER-2/neu (column 14, lines 47-57).
As relating to claim 78, Lane et al. teach the antigen to be CD25 (page 2, paragraph 25, and page 12, paragraph 133).
Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare the above taught composition in an effective amount as taught by the applicant having the above-cited references before him. It is well known in the art that glucan works by activating the immune system in response to a myriad of factors, including many types of foreign cells and intigens--viruses, bacteria, and various types of cancer. Specifically, glucan mimics the natural physiologic response to an infectious challenge by enhancing the balanced, endogenous release of cytokines (James et al.). By considering the teaching of James et al. and Dorothee Herlyn, it would lead one skilled in the art to have a reasonable expectation of success in combining the method for producing high molecular weight, soluble glucan polymers taught by James et al. with the teachings of Dorothee Herlyn, Marciani et al, Yan et al., Chu et al., Cheever et al, and Lane et al. to treat infectious and autoimmune diseases, including enhancing efficacy of antibodies against many types of cancer. One skilled in the art would be motivated to combine these two teachings to obtain a less

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International application No.
PCT/US04/23099

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

evasive, more convenient cancer fighting regiment that included oral administration of tumor fighting agents, and thus overcome what was once a significant impediment in the art.